In the Specification:

Please amend the specification as shown:

Please delete paragraph [00046] on page 12, and replace it with the following paragraph:

--**[00046]** a molecule including a binding region of JNKK2 characterized by the amino acid sequence from positions 132-156 **of SEQ ID NO: 50** (GPVWKMRFRKTGHVIAVKQMRRSGN) the full length JNKK2; and--

Please delete paragraph [00047] on page 12, and replace it with the following paragraph:

--**[00047]** a molecule including a binding region of JNKK2 characterized by the amino acid sequence from positions 220-234 **of SEQ ID NO: 50** (GKMTVAIVKALYYLK) of the full length JNKK2.--

Please delete paragraph [00083] on page 28, and replace it with the following paragraph:

--**[00083]** FIG. 29 shows that MKK7 contacts Gadd45β through two petidic regions in its catalytic domain. a, c, e, are schematic representations of the MKK7 N- and C-terminal truncations and peptides, respectively, used for binding assays. Interaction regions are shaded in gray. b, d, f, GST are pull-downs showing GST-Gadd45 β binding to the indicated 35S-labeled, *in vitro* translated MKK7 products. Shown is 40% of the inputs. g, is an amino acid sequence of Gadd45β -interacting peptides 1 **(residues 132-156 of SEQ ID NO: 50)** and 7 **(residues 220-234 of SEQ ID NO: 50)**. K149 is highlighted.--

Please delete paragraph [00085] on page 28, and replace it with the following paragraph:

--**[00085]** FIG. 31 (A-D) **(SEQ ID NOS 49-52, respectively, in order of appearance)** shows nucleotide and amino acid sequences of human and murine JNKK2.--

Please delete paragraph [000164] on page 59, and replace it with the following paragraph:

--**[000164]** For caspase *in vitro* assays, cells were lysed in Triton X-100 buffer and lysates incubated in 40μM of the following amino trifluromethyl coumarin (ATC)-labeled caspase-

specific peptides (Bachem): xVDVAD **(SEQ ID NO: 42)** (caspase 2), zDEVD **(SEQ ID NO: 43)** (caspases 3/7), xVEID **(SEQ ID NO: 44)** (caspase 6), xIETD **(SEQ ID NO: 45)** (caspase 8), and Ac-LEHD **(SEQ ID NO: 46)** (caspase 9). Assays were carried out as previously described (Stegh *et al.*, 2000) and specific activities were determined using a fluorescence plate reader. Mitochondrial transmembrane potential was measured by means of the fluorescent dye JC-1 (Molecular Probes, Inc.) as previously described (Scaffidi *et al.*, 1999). After TNFα treatment, cells were incubated with 1.25 μg/ml of the dye for 10 min at 37°C in the dark, washed once with PBS and analyzed by FCM.--

Please delete paragraph [000220] on pages 76-77, and replace it with the following paragraph:

--**[000220]** The pMT2T, pMT2T-p50, and pMT2T-RelA expression plasmids were described previously (Franzoso *et al.*, 1992). To generate the *gadd45β*-CAT reporter constructs, portions of the *gadd45β* promoter were amplified from pBS-014D by polymerase chain reaction (PCR) using the following primers: 5'-GGATAACGCGTCACCGTCCTCAAACTTACCAAACGTTTA-3'(SEQ ID NO: 16) and 5'-GGATGGATATCCGAAATTAATCCAAGAAGACAGAGATGAAC-3' **(SEQ ID NO: 17)** (-592/+23-*gadd45β*, MluI and EcoRV sites incorporated into sense and anti-sense primers, respectively, are underlined); 5'-GGATAACGCGTTAGAGCTCTCTGGCTTTTCTAGCTGTC-3' **(SEQ ID NO: 18)** and 5'-GGATGGATATCCGAAATTAATCCAAGAAGACAGAGATGAAC-3' **(SEQ ID NO: 19)** (-265/+23-*gadd45β*); 5'-GGATAACGCGTAAAGCGCATGCCTCCAGTGGCCACG-3' **(SEQ ID NO: 20)** and 5'- GGATGGATATCCGAAATTAATCCAAGAAGACAGAGATGAAC-3' **(SEQ ID NO: 21)** (-103/+23-*gadd45β*); 5'-GGATAACGCGTCACCGTCCTCAAACTTACCAAACGTTTA-3' **(SEQ ID NO: 22)** and 5'-GGATGGATATCCAAGAGGCAAAAAAACCTTCCCGTGCGA-3' **(SEQ ID NO: 23)** (-592/+139-*gadd45β*); 5'-GGATAACGCGTTAGAGCTCTCTGGCTTTTCTAGCTGTC-3' **(SEQ ID NO: 24)** and 5'- GGATGGATATCCAAGAGGCAAAAAAACCTTCCCGTGCGA-3' **(SEQ ID NO: 25)** (-265/+139-*gadd45β*). PCR products were digested with MluI and EcoRV and ligated into the MluI and SmaI sites of the promoterless pCAT3-Basic vector (Promega) to drive

ligated into the MluI and SmaI sites of the promoterless pCAT2-Basic vector (Promega) to drive expression of the chloramphenicol acetyl-transferase (CAT) gene. All inserts were confirmed by sequencing. To generate -5407/+23-*gadd45β*-CAT and -3465/+23-*gadd45β*-CAT, pBS-014D was digested with XhoI or EcoNI, respectively, subjected to Klenow filling, and further digested with BssHII. The resulting 5039 bp XhoI-BssHII and 3097 bp EcoNI-BssH II fragments were then independently inserted between a filled-in MluI site and the BssHII site of -592/+23-*gadd45β*-CAT. The two latter constructs contained the *gadd45β* promoter fragment spanning from either -5407 or -3465 to -368 directly joined to the -38/+23 fragment. Both reporter plasmids contained intact κB-1, κB-2, and κB-3 sites (see FIG. 10).--

Please delete paragraph [000221] on pages 77-78, and replace it with the following paragraph:

--**[000221]** κB-1M-*gadd45β*-CAT, κB-2M-*gadd45β*-CAT, and κB-3M-*gadd45β*-CAT were obtained by site-directed mutagenesis of the -592+23-*gadd45β*-CAT plasmid using the QuikChange™ kit (Stratagene) according to the manufacturer's instructions. The following base substitution were introduced: 5'-TAGGGACTCTCC-2' **(SEQ ID NO: 26)** to 5'-**AATATT**CTCTCC-3' **(SEQ ID NO: 27)** (κB-1M-*gadd45β*-CAT; κB sites and their mutated counterparts are underlined; mutated nucleotides are in bold); 5'-GGGGATTCCA-3' **(SEQ ID NO: 28)** to 5'-**ATC**GATTCCA-3' **(SEQ ID NO: 29)** (κB-2M-*gadd45β*-CAT); and 5'-GGAAACCCCG-3' **(SEQ ID NO: 30)** to 5' - GGAAA**TATTG** - 3' **(SEQ ID NO: 31)** (κB-3M-*gadd45β*-CAT). κB-1/2-*gadd45β*-CAT, containing mutated κB-1 and κB-2 sites, was derived from κB-2M-*gadd45β*-CAT by site-directed mutagenesis of κB-1, as described above. With all constructs, the -592/+23 promoter fragment, including mutated κB elements, and the pCAT-3-Basic region spanning from the SmaI cloning site to the end of the CAT poly-adenylation signal were confirmed by sequencing.--

Please delete paragraph [000222] on page 78, and replace it with the following paragraph:

--**[000222]** Δ56-κB-1/2-CAT, Δ56-κB-3-CAT, and Δ56-κB-M-CAT reporter plasmids were constructed by inserting wild-type or mutated oligonucleotides derived from the mouse *gadd45β*

promoter into Δ56-CAT between the BglII and XhoI sites, located immediately upstream of a minimal mouse *c-fos* promoter. The oligonucleotides used were: 5'-GATCTCTAGGGACTCTCCGGGGACAGCGAGGGGATTCCAGACC- 3' **(SEQ ID NO: 32)** (κB-1/2-CAT; κB-1 and κB-2 sites are underlined, respectively); 5'-GATCTGAATTCGCTGGAAACCCCGCAC-3' **(SEQ ID NO: 33)** (κB-3-CAT; κB-3 is underlined); and 5' - GATCTGAATTCTACTTACTCTCAAGAC- 3' **(SEQ ID NO: 34)** (κB-M-CAT).--

Please delete paragraph [000235] on pages 81-82, and replace it with the following paragraph:

--**[000235]** In vitro transcription and translation reactions were carried out by using the TNT coupled reticulocyte lysate system (Promega) according to the manufacturer's instructions in the presence of [^{35}S]methionine. To prime *in vitro* reactions, cDNAs were cloned into the pBluescript (pBS) SK- plasmid (Stratagene). FL murine MEKK4 was cloned into the SpeI and EcoRI sites of pBS and was transcribed with the T3 polymerase; FL human JNKK2, FL murine JNKK1, and FL human ASK1, were cloned into the XbaI-EcoRI, NotI-EcoRI, and XbaI-ApaI sites of pBS, respectively, and were transcribed by using the T7 polymerase. pBS-C-ASK1 - encoding amino acids 648-1375 of human ASK1 - was derived from pBS-FL-ASK1 by excision of the EarI and XbaI fragment of ASK1 and insertion of the following oligonucleotide linker: 5'-CGCCACCATGGAGATGGTGAACACCAT-3' **(SEQ ID NO: 47)** . N-ASK1 - encoding the 1-756 amino acid fragment of ASK1 - was obtained by priming the in vitro transcription/translation reaction with pBS-FL-ASK1 digested with PpuMI.--

Please delete paragraph [000237] on page 82, and replace it with the following paragraph:

[000237] To generate Gadd45β polypeptides, *in vitro* reactions were primed with pBS-GFP-Gadd45β plasmids, encoding green fluorescent protein (GFP) directly fused to FL or truncated Gadd45β. To obtain these plasmids, pBS-Gadd45β(FL), pBS-Gadd45β(41-160), pBS-Gadd45β(60-160), pBS-Gadd45β(69-160), pBS-Gadd45β(87-160), and pBS-Gadd45β(113-160) - encoding the corresponding amino acid residues of murine Gadd45β were generated - by

cloning appropriate *gadd45β* cDNA fragments into the XhoI and HindIII sites of pBS SK-. These plasmids, encoding either FL or truncated Gadd45β, were then opened with KpnI and XhoI, and the excised DNA fragments were replaced with the KpnI-BsrGI fragment of pEGFP-N1 (Clontech; containing the GFP-coding sequence) directly joined to the following oligonucleotide linker: 5'-GTACAAGGGTATGGCTATGTCAATGGGAGGTAG-3' **(SEQ ID NO: 48)**. These constructs were designated as pBS-GFP-Gadd45β. Gadd45β C-terminal deletions were obtained as described for the JNKK2 deletions by using pBS-GFP-Gadd45β(FL) that had been digested with the NgoMI, SphI, or EcoRV restriction enzymes to direct protein synthesis in vitro. These plasmids encoded the 1-134, 1-95, and 1-68 amino acid fragments of Gadd45β, respectively. All pBS-Gadd45β constructs were transcribed using the T7 polymerase.

Pages 87-101, please delete the Sequence Listing as originally filed, replacing with the Sequence Listing filed concurrently herewith, and renumber pages 102-111 sequentially thereafter.